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PRESERVATION OF HIGH-ORDER FUNCTION IN ISOLATED SOMATIC CORTEX IN CALLOSUM-SECTIONED CAT[1]

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DISCRIMINATIVE LEARNING AND memory have been found to proceed independently in the separate hemispheres in the cat following section of the corpus callosum (2–4, 6–10). In the absence of callosal function tactile discriminations learned with one forepaw or pattern discriminations learned with one eye (the optic chiasma being sectioned in the midline) must be relearned completely when the animal is forced to use the contralateral forepaw or eye.

This functional independence of the two hemispheres in the callosum-sectioned cat has been put to use in the present study in an effort to test the functional capacity of the surgically isolated somatic cortex. The experimental plan involved removal of the greater part of the neocortex on one side leaving only the frontal region with its somatic sensory and motor areas. The callosum was sectioned completely and the other hemisphere was left sufficiently intact to avoid incapacitating paralysis and to maintain generalized motor and other non-test activities. The functional capacity of the isolated frontal cortex was tested in terms of the animals' ability to retain and to learn somesthetic discriminations with the contralateral forepaw.

METHOD

Animals. Four adult cats were used that ranged in age from 17 to 21 months at the start of the experiment. All four had been trained in an earlier study (10) to perform softness, form, and roughness discriminations, S-H, W-F, and R-S as illustrated below. In two cases, *Hrr* and *Bnj*, the corpus callosum had already been sectioned in the preceding study.

Surgery. Anesthesia was established by intrapleural injection of Nembutal (0.4 cc./lb.). All operations were performed with the aid of a ball-joint, mandible mold headholder developed by the author. The callosum was sectioned by opening the skull widely on one side and retracting the hemisphere of the same side, the unretracted hemisphere being reserved for the cortical removal. The hippocampal commissure was sectioned in all cases along with the callosum. The anterior commissure was left intact. The cortical removals were carried out by gentle suction and the removed cortex was replaced with a mixture of Gelfoam and polyethylene sponge. The larger portions of removed skull plate were replaced and fastened with tantalum sutures. A stereoscopic microscope was used for all the finer parts of the surgery.

Functional tests. The apparatus and general procedure for the training and testing of unilateral forepaw discriminations was the same as used previously (10). In brief, the cats

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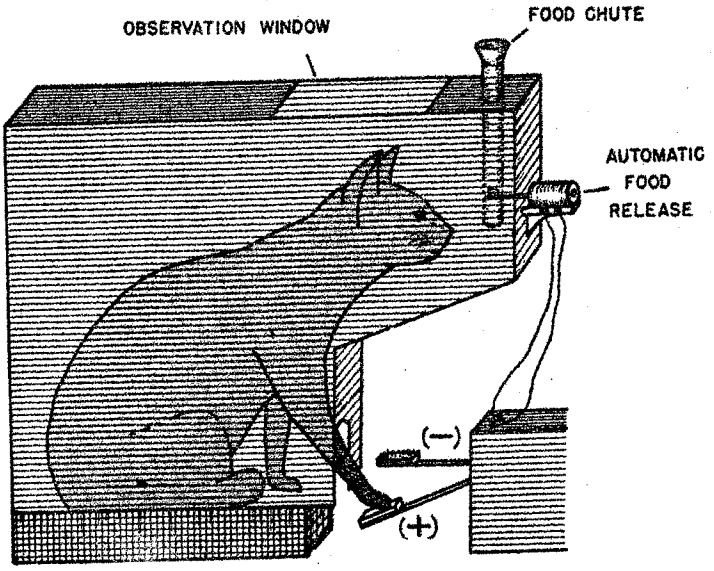

FIG. 1. Simplified sketch of testing apparatus. Depression of correct pedal releases morsel of food; incorrect pedal activates buzzer. Right-left position of correct pedal shifted at random.

were trained to push the correct one of two pedals which they were able to reach with only one forepaw and which they were unable to see and had to distinguish entirely on the basis of touch (see Fig. 1). Different pairs of mountings on the pedals used for different types of discriminations are shown in Fig. 2 where they are arranged in the approximate

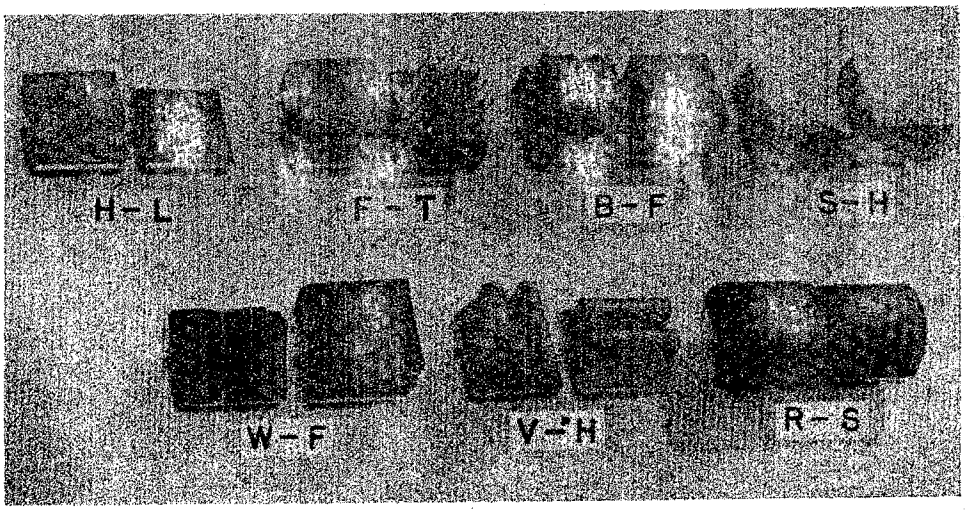

FIG. 2. Pairs of pedal mountings used to test somesthetic discrimination. Left one of each pair was rewarded except in F-T. H-L, high vs. low pedal. F-T, flat wood vs. tines of plastic. B-F, bristles vs. flat wood. S-H, soft rubber vs. wood, both cloth covered. W-F, wedge-shaped block vs. flat block, both plastic covered. V-H, vertical vs. horizontal wooden ridges. R-S, rough #7 sandpaper vs. smooth wood, both half cylinders.

order of increasing difficulty from left to right as judged by the number of trials required for learning. Similarities in the negative pedal in F-T, B-F, S-H, and W-F made for reinforcement of learning in varying degree within this series. After a discrimination was learned (criterion of learning was 17 correct out of 20 consecutive trials or the statistical equivalent), the performance was stabilized by overtraining 200–300 trials. One of the simpler of the learned discriminations was reserved in each case for preliminary testing during recovery from surgery to use for estimating the course of diaschisis and to help maintain the general adaptation to the testing apparatus. After the animals had recovered from surgery to the point where they were able to perform their preliminary task, they were tested for retention of the other discriminations and for their ability to learn additional new discriminations. The series of operations and functional tests extended over a period of 14 months. Just prior to each surgical intervention sufficient practice was given to assure a good preoperative performance level with which to compare the postoperative performance.

Examination of brains. Following postmortem perfusion of the head with 10% formalin, the brain was removed and preserved in 10% formalin. The completeness of callosal section was verified by gross inspection and the extent of the other lesions was determined grossly and recorded in photographs, some of which are shown in Fig. 4. After their division in the midsagittal plane the brains of *Jsp*, *Hrr*, and *Frn* were embedded in paraffin, sectioned at 15 mμ, and stained with thionin and by the Weil procedure.

Observations

Initial isolation of right frontal region. Removal of the right cerebral cortex was carried out in all four cases to approximately the extent indicated in Fig. 3. During the first week after operation discrimination with the affected left forepaw was absent in all cases. Discriminative performance on the preliminary problem H-L began to reappear during the 3rd week and improved rapidly during the 4th and 5th weeks.

When good performance on the preliminary task had been regained, at about 26–32 days after the cortical removal, the cats were tested for retention of the three preoperatively trained discriminations S-H, W-F, and R-S. All cases exhibited good-to-excellent retention of the first two. Discrimination R-S, however, had to be relearned in large part. Its reestablishment required from half to two-thirds as many training trials as had the initial learning. This discrimination had been the most difficult of the three tests in terms of the number of trials required for initial learning (10), and it tended to be forgotten more rapidly than the others when not reinforced by training. Thus the partial loss of discrimination R-S could be ascribed, in part at least, to normal memory loss.

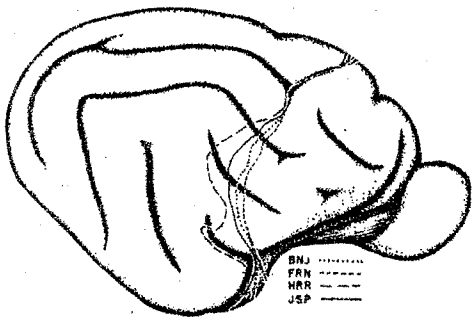

Fig. 3. Extent of cortical removal in right hemisphere as estimated from removed brains. Lines indicate posterior edge of intact frontal area. Medial extension of lesions approximated that of *Frn* illustrated in Fig. 4.

The capacity to learn new discriminations with the affected forepaw was tested with discriminations B-F and V-H. All four cases learned the first of these easily in 30–90 trials. The latter and more difficult problem, presented only to *Hrr* and *Jsp*, was learned in 480 and 150 trials respectively. The problem B-F was then trained on the other side. With the right paw the number of trials required for learning was of the same order as with the left in *Hrr* and *Bnj*. In *Frn* and *Jsp* learning with the right paw required less than two-thirds as many trials as with the left paw, owing presumably to partial transfer through the callosum which was still unsectioned in these two cases. Problem V-H was learned on the right side in 360 trials by *Hrr* and in 130 trails by *Jsp*. After completion of the foregoing, the callosum was sectioned in *Frn* and *Jsp*. Retention tests were started at 18 and 20 days respectively after this operation, by which time good performance had been reinstated on the preliminary discrimination H-L. Tests on all the other trained discriminations conducted through the 26th day failed to reveal any significant effect of the callosum section upon the performance with either paw.

Because the most difficult of the test discriminations, R-S, had by this time been found to require rather frequent reinforcement by training even in normal cats to prevent its loss, regardless of surgical intervention, and because the sandpaper surface wore off and had to be renewed frequently, this discrimination was dropped from further testing in the remainder of the experiment.

Additional reduction of right cortical remnant. The portion of the remaining intact cortex on the medial surface of the right hemisphere was next removed in cases *Jsp*, *Hrr*, and *Frn*. The aim was to eliminate the medial portions of the anterior and posterior sigmoid gyri plus the upper portion of G. proreus and genualis. The removals were made rather blindly through a dorsomedial opening in the skull overlying the posterior sigmoid gyrus.

Performance on H-L was recovered in all three cases between 5 and 15 days after this removal. During the third week after the operation *Jsp* and *Frn* exhibited good retention of all their learned discriminations, excepting R-S which had been dropped from the tests for reasons indicated above. In case *Hrr*, retention was not as good as in *Jsp* and *Frn*. The performance on discriminations B-F, S-H and W-F remained highly erratic through the first 4 weeks after operation. Discrimination V-H, presented to *Hrr* during the 6th week after operation, was not remembered but was relearned in 395 trials. It was later found that the removal of medial cortex had been somewhat more extensive in *Hrr* than in *Jsp* and *Frn*, particularly in its lateral extension in the region on the sigmoid fissure. Eventually the performance of *Hrr* with the left paw became more steady until, by the end of the 2nd month, all the discriminations were being performed with 81–92 correct trials out of 100.

No marked impairment was evident at this stage in any of the above three cases in their ability to learn additional new discriminations with the left paw. F-T was learned in less than 90 trials with the left paw by all three

animals, the rapid learning being attributable in part to the simplicity of the problem and in part to its similarity to the previously learned B-F. The much more difficult task, V-H, given to *Frn* for the first time, was learned in 490 trials with the left paw.

As a preparation for retention tests following lesions to be made in the left cortex, some of the new discriminations were trained to the right paw. F-T was learned rapidly in less than 80 trials in all three cases on the right side. The more difficult V-H was learned on the right by *Hrr* and *Frn* in 270 and 410 trials respectively.

Elimination of right cortical remnant. A more drastic reduction was effected in the size of the cortical remnant in *Bnj*, including removal of tissue around the greater part of the periphery of the intact island. This abolished all discriminative performance with the left paw. Eight weeks after operation the use of the left paw was still so extremely defective as to indicate that probably none of the test discriminations would be recovered. There was motor involvement as well as sensory, but the cat did not make any attempt to push the pedals. It was sacrificed at the end of the 8th week. Upon examination of the brain the remains of a large blood clot was found that had invaded extensively the white matter underneath the remaining cortical island, the effects of which must have eliminated the function of most of the fibers passing to and from the whole sigmoid area.

Lesions in sensorimotor field of contralateral (left) hemisphere. In *Jsp* a small contralateral lesion was made, which affected only the central foreleg part of somatic area I, especially the more posterior portion (see Fig. 4F). Between the 10th and 14th days after the operation, motor performance of the right forepaw with apparent sensory testing was present but correct discrimination on F-T was absent. The performance of the *left* foot was then tested between the 14th and 19th days after operation and was found to be unimpaired on all discriminations.

When the right foot was again tested on the 22nd and 23rd days after operation, discrimination of S-H was performed without difficulty. However, the scores on the more difficult W-F remained no better than chance throughout 90 trials. When the right foot was next tested on day 33, discrimination W-F had been recovered. The performance on the more difficult V-H remained no better than chance throughout 200 trials during the next 3 days. By the 63rd day after operation, and in the course of 700 training trials, *Jsp* was finally able to relearn discrimination V-H with the right paw.

In *Hrr* a larger lesion was made in the left cortex, roughly equivalent in extent to the intact cortical remnant left on the right side, but not involving the medial surface of the hemisphere nor the lower depths of the cruciate sulcus (Fig. 4G). This abolished the pedal-pushing responses on both sides during the following 3 weeks. The effect on the performance with the left paw during this period was apparently a secondary one attributable to the postural defects associated with the generalized ataxia on the right side. The cat during this period would test the two pedals with the left paw, choose the

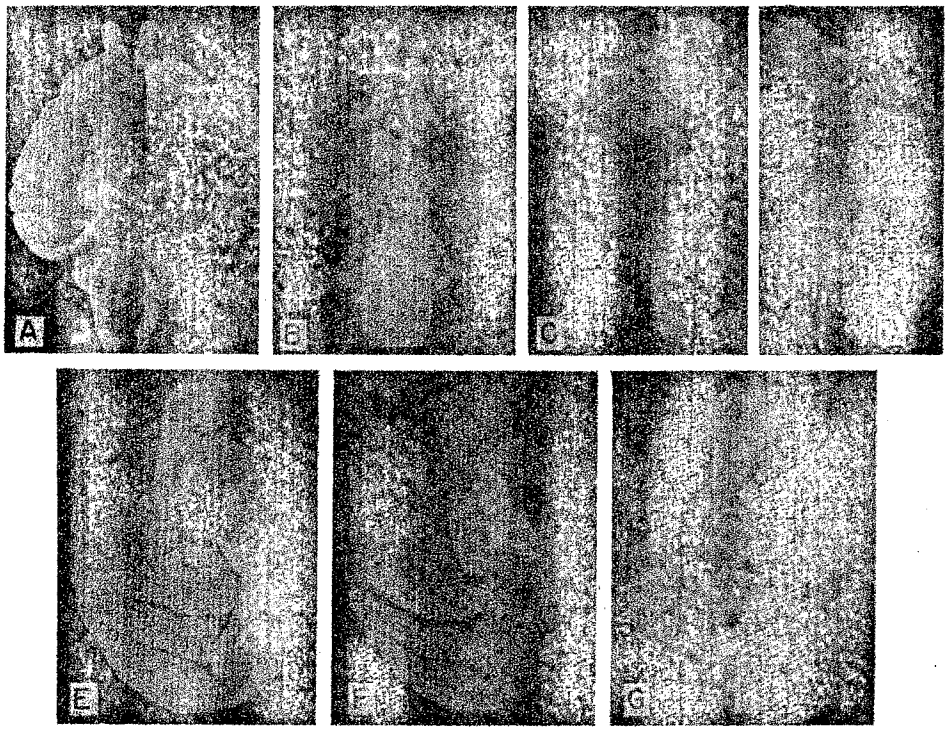

FIG. 4. A–D: photographs of brain of *Frn* cleared of membranes and scar tissue to show extent of intact right cortex. E–G: lesions in left hemisphere of *Frn*, *Jsp*, and *Hrr* respectively with lesion surfaces tinted by iron haematoxylin.

correct one, and push it repeatedly, but was unable to exert enough pressure to trip the electric switch. The general posture during this performance was quite abnormal, with the right forepaw being hooked high on the food platform alongside the head instead of being placed on the floor for support in the usual manner employed prior to this last operation.

By the 30th day after the cortical removal, *Hrr* was again performing well with the left foot on F-T. Discrimination tests B-F, W-F, S-H, and V-H were then presented in that order during the next 4 days and all were performed without difficulty with the left foot. Performance with the left paw was maintained during the subsequent 4 weeks during which time the right foot was tested at irregular intervals. There was little or no improvement in the use of the right paw. During the 5th and 6th weeks a final effort was made to reestablish discriminative performance with the right paw by intensive testing on discrimination F-T but no progress was evident. On rare occasions the cat reached out and pushed at the pedals, but there was no sign of any discrimination.

In this final stage, *Hrr* was still able, in the course of generalized testing, to reach out accurately with the left, and somewhat less accurately with the

right, forepaw for small pieces of food, less than 2 cm. lengthwise, presented within reaching distance in front near the midline. These eye-paw responses were accurately aimed also when the cat was lying on its back and while it was chasing erratically moving objects like a flying moth or a small ball of aluminum foil. Visual placing reactions were obtained from both forefeet. Visual centering and following movements were strong and the cat had no difficulty making its way through a maze of obstacles set up in an unfamiliar room. All the foregoing visual reactions were abolished when the left eye was blinded with a rubber mask. Placing reactions elicited by contact with chin and dorsum of forepaw, the left eye being masked, were present on both sides. Supporting and hopping reactions were obtained with the left forefoot, but not with the right. In its final state, *Hrr* was excessively active, exhibiting continuous pacing and much treading, but the cat remained healthy, vigorous and normal in temperament.

In *Frn* a lesion was made in the left somatic cortex somewhat smaller in size than that made on the left in *Hrr* but larger than the left lesion in *Jsp* (see Fig. 4E). Tests conducted on the 20th and 24th days after operation demonstrated complete loss of all the trained discriminations performed with the right paw whereas those performed with the left paw were retained at a high level. On the left there was an appreciable loss only on problem V-H for which 130 trials were required to reach criterion. It is questionable that this small relapse on V-H was significant as an effect of the cortical lesion.

The right paw was given further testing on the simple discrimination F-T through the 56th day after operation, including a total of 1,000 trials. The attainment of criterion at three different points in the course of the thousand trials indicated that a trace of discriminative capacity remained. However, the performance was erratic and an above-chance score could not be maintained. The cat at this stage was quite able to push the pedals with the right paw but had difficulty selecting the correct one to push. The presence of a trace of discrimination with the right paw was verified in further testing on W-F during the succeeding 3 weeks. Again criterion was achieved sporadically a few times in the course of 450 trials. For some unknown reason W-F seemed to be the easiest of the discriminations for *Frn* with both right and left paws in these later stages of the experiment. Finally *Frn* was given an additional 200 trials on S-H but failed to make criterion.

In generalized tests of visuomotor coordination involving reaching, placing, centering, following and jumping reactions, *Frn's* performance was similar to that of *Hrr* except that the use of the right forepaw was somewhat less impaired than in *Hrr* and the tests could be performed with either eye. With both eyes masked, placing reactions elicited by contact with chin or dorsum of the foot were present on both sides as were hopping and supporting reflexes. The hyperactivity seen in *Hrr* was not present in *Frn*.

Finally an effort was made to see if *Jsp* with intact visual cortex on the left, surgically isolated from the intact somatic cortex on the right, could select and push the correct pedal on the basis of vision. The opaque panel

that screened the pedals was removed from the apparatus and one pedal was painted with vertical and the other with horizontal stripes. An attempt was made to teach *Jsp* to select the pedal with vertical stripes. No progress was apparent at the end of 400 trials in 5 days. Various things were tried to attract visual attention to the pedals, but the cat continued in a rigidly fixed manner to try to select the pedals by touch alone. It was concluded that the answer to this latter question should be sought in animals pretrained from the start to select in terms of vision rather than touch.

Anatomical examination

The corpus callosum and hippocampal commissure were found to have been completely sectioned in all four cases. The section of the chiasma in *Hrr* also was complete. The extent to which the neocortex had been removed is indicated grossly in Figs. 3 and 4. In *Hrr* the cortex in the lower medial depths of the cruciate sulcus on the left side was found intact and may have been functional. The pyriform lobe was partially damaged on the right side in all but *Hrr*, being mostly removed in *Frn* except for a medial remnant. The hippocampus on the right showed little or no damage and the columns of the fornix on the same side remained intact and apparently functional. The fornix on the left side was partially interrupted in *Hrr* and *Jsp*. In all four cases there was damage in the dorsal part of the septal area on the left side, but little or none on the right. The amygdaloid complex was spared in the main except in *Frn* where the bulk of the amygdaloid was destroyed anterior and adjacent to the optic tract. Otherwise the lesions had not invaded significantly the basal ganglia or thalamus. In the three brains sectioned, severe retrograde degeneration was present on the right side in lateral and medial geniculate nuclei, in the pulvinar, and in lateralis dorsalis and lateralis posterior. Extensive degeneration was evident also in the right anterior nuclei, particularly in anterior ventralis. In the left thalamus degeneration was centered in posterolateralis with involvement of ventralis lateralis and posteromedialis, these being affected increasingly in *Frn* and *Hrr* in that order. In *Hrr* medialis dorsalis also showed degeneration on the left.

Discussion

The results show that in the callosum-sectioned cat somesthetic discriminations performed with the left forepaw may be retained at a high level and additional new discriminations can be learned readily following removal from the right hemisphere of all neocortex excepting the small frontal area illustrated in Fig. 4. This cortical remnant was sufficient for high-level retention and new learning of these discriminations and, conversely, removal of the same area on the contralateral side permanently abolished the discriminations on that side. Accordingly it would appear that the specific cortical reorganizations and mnemonic changes involved in the establishment and maintenance of the discrimination habits performed with the left paw were localized mainly or entirely within the cortical remnant.

The results indicate little, if any, mnemonic contribution from the homolateral cortex. This is suggested in the complete loss of discrimination produced by destruction of the right cortical remnant in *Bnj*, and also by the survival in the other cases of discrimination with the left paw and the loss with the right paw following removals from the corresponding cortical area in the intact left hemisphere. The possibility of subcortical engrams for these habits is not ruled out but seems unlikely, especially as these same habits had failed to transfer in these cats after callosal section (10). The results are in

accord with the effect on somesthetic discrimination produced by bilateral removals of somatic I and II in the cat (11).

The capacity of the cortical island to mediate the learning of new discriminations was remarkably unimpaired. Controlled comparisons between learning rate for the right cortical remnant and that for the intact left hemisphere were not made, but the data obtained indicated that they were grossly of the same order. Similarly, no gross differences were evident, within the range of the experimental tests, between cortical island and intact hemisphere in regard to the capacity to retain the trained discriminations once they had been learned.

The present findings are not in accord with similar isolation of the visual cortex in the chiasma-callosum sectioned cat (6, 7). In the visual sphere perceptual learning and memory seem to be considerably impaired by similar surgical isolation for reasons yet unknown. The retention of accurate visuomotor coordination in *Hrr* in the final stage of the experiment is in line with unpublished observations of Myers, Sperry, and Miner that accurate eye-paw coordination survives removal of the frontal cortex with all of somatic I and II from one hemisphere plus removal of the entire temporal, occipital, and posterior parietal areas from the other hemisphere in cats with total section of corpus callosum, optic chiasma, and anterior and hippocampal commissures. It means that visually guided voluntary forelimb coordination is dependent upon only the most indirect kind of communication, if any, between visual and motor cortex. The finding conforms with changing views of rolandic function as expressed by Denny-Brown (1), and by Penfield (5) in his outline for a centrencephalic system in volitional activity—with the reservation that the bilaterality of the centrencephalic relations, in the cat at least, is not sufficient to effect interhemispheric transfer of learned information.

Summary

After the right sensorimotor cortex had been surgically isolated in four callosum-sectioned cats to the extent shown in Figs. 3 and 4, the cats retained their ability to perform preoperatively trained somesthetic discriminations at high level with the left forepaw. Also, they showed no marked retardation in ability to use the affected left paw to learn new discriminations.

An attempt further to reduce the size of the cortical remnant abolished completely in one case all discriminative performance with the affected paw.

Cortical lesions centered in the somatic area of the left hemisphere abolished or severely impaired discriminative performance with the right paw, but left unaffected that with the left paw.

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